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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,618	05/05/2006	Brenda F. Baker	CORE0005USA	9771
32650	7590	07/02/2007	EXAMINER	
WOODCOCK WASHBURN LLP			VIVLEMORE, TRACY ANN	
CIRA CENTRE, 12TH FLOOR				
2929 ARCH STREET				
PHILADELPHIA, PA 19104-2891			ART UNIT	PAPER NUMBER
			1635	
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			07/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/561,618	BAKER, BRENDA F.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Tracy Vivlemore	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 20 April 2007.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-11, 14, 15, 17, 19, 24, 30-34, 38, 40 and 57-60 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-11, 14, 15, 17, 19, 24, 30-34, 38, 40 and 57-60 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
  1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 8/06.
- 4) Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) Notice of Informal Patent Application
- 6) Other: \_\_\_\_\_.

**DETAILED ACTION**

***Election/Restrictions***

Applicant's election of species of 2'-F as an affinity enhancing sugar modification and inosine as an affinity decreasing base modification in the reply filed on April 20, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-11, 14, 15, 17, 19, 24, 30-34, 38, 40, and 57-60 are pending and under examination.

***Claim Objections***

Claim 2 is objected to because of the following informalities: the amendment to this claim striking through a portion of the text has included the period ending the sentence, removing it from the claim. Appropriate correction is required.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States

Art Unit: 1635

only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-7, 9, 10, 14, 15, 17, 19, 24, 30, 38 and 40 are rejected under 35 U.S.C. 102(e) as being anticipated by Fosnaugh et al. (US 2003/0143732).

The claims are directed to compositions of first and second oligomeric compounds wherein a portion of the first oligomeric compound is complementary to and capable of hybridizing to a target nucleic acid, at least 18 nucleosides of the first oligomeric compound hybridizes to the second oligomeric compound. One compound comprises at least one sugar modified nucleoside having enhanced affinity relative to an unmodified  $\beta$ -D-ribonucleoside and the other compound comprises at least one base modified nucleoside having enhanced or decreased affinity relative to an unmodified  $\beta$ -D-ribonucleoside. Specific embodiments recite the location of the sugar modified nucleotide, the location of the modification within a purine or pyrimidine and the identity of the modification. Other embodiments recite the identity of the sugar modification and the length of the oligomeric compounds.

Fosnaugh et al. disclose siRNAs that are about 19 to about 25 nucleotides in length and comprise an antisense region complementary to a sequence encoding a target RNA and a sense region complementary to the antisense region. The siRNA molecule can comprise two separate nucleic acid fragments or the sense and antisense regions can be covalently connected via a polynucleotide linker or a non-nucleotide linker. At paragraph 34 Fosnaugh et al. disclose chemically modified siRNAs, with chemical modifications including 2'-deoxy-2'-fluoro ribonucleotides, "universal base"

Art Unit: 1635

nucleotides and 5-methyl-C nucleotides, which improve the stability of the interaction with the target RNA sequence and to improve nuclease resistance. Other modified bases are disclosed at paragraph 43, including 2,6-diaminopurine or "any other non-naturally occurring base that can be employed to be complementary or non-complementary to...RNA or a non-nucleosidic base such as phenyl, naphthyl, 3-nitropyrrole, 5-nitroindole, nebularine, pyridone, pyridinone, or any other non-naturally occurring universal base that can be complementary or non-complementary to...RNA." At paragraph 50 it is specifically disclosed that 2'-deoxy-2'-fluoro modified nucleotides and universal base modifications can be present in either the sense strand, the antisense strand or both strands. Universal base is defined at paragraph 129 as including inosine while at paragraph 186 the term "nucleotide" is disclosed as including both natural bases and the modified bases known in the art and at paragraph 171 it is disclosed that siRNAs can also include one or more LNA nucleotides. While Fosnaugh et al. do not specifically recite that 2'-fluoro modifications provide enhanced affinity relative to an unmodified ribonucleoside and do not specifically recite modified nucleobases having enhanced or decreased affinity relative to an unmodified ribonucleoside, Fosnaugh et al. disclose specific siRNA structures meeting the limitations of the instant claims and therefore these modification are assumed, absent evidence to the contrary, to inherently possess these characteristics.

Thus, Fosnaugh et al. disclose all limitations of and anticipate claims 1-7, 9, 10, 14, 15, 17, 19, 24, 30, 34, 38 and 40.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-11, 14, 15, 17, 19, 24, 30-34, 38, 40 and 57-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fosnaugh et al. as applied to claims 1-7, 9, 10, 14, 15, 17, 19, 24, 30, 34, 38 and 40 above, and further in view of Langel et al. (US 6,025,140) and Lin et al. (US 6,414,127).

Claims 1-7, 9, 10, 14, 15, 17, 19, 24, 30, 34, 38 and 40 are described in the 102 rejection over Fosnaugh et al. Claims 8 and 11 recite particular modified nucleotides. Claims 31-33 recite that each of the 2' substituents is 2'-F. Claims 57-60 recite particular embodiments wherein each of the 2' substituents is 2'-F and the other strand comprises an affinity-decreasing base modification that may be inosine.

The teachings of Fosnaugh et al. are described in the 102 rejection over this reference. Fosnaugh et al. teach modifications to nucleotides in a permissive manner, describing at paragraph 43 for example that a siRNA can comprise any naturally or non-naturally occurring nucleobase and also describing at paragraph 50 that a siRNA can comprise "5 or more" 2'-fluoro nucleotides, but Fosnaugh et al. does not explicitly teach a siRNA comprising 2-thioU or 2-thioC or a siRNA wherein every position contains a 2'-fluoro modified nucleotide. Fosnaugh et al. further teach at paragraph 171 that siRNAs

can include G-clamp nucleotides, a modified cytosine analog that confers the ability to hydrogen bond both Watson-Crick and Hoogsteen faces of a complementary guanine within a duplex, resulting in substantially enhanced helical thermal stability and mismatch discrimination when hybridized to complementary oligonucleotides. While the description of G-clamp nucleotides refers to the initial publication by Matteucci et al., Fosnaugh et al. do not explicitly teach a G-clamp nucleotide wherein the R<sub>11</sub> position is defined as in claim 11.

Numerous modified nucleobases were known to those of ordinary skill in the art at the time the invention was made. For example, Langel et al. teach antisense oligonucleotides comprising nucleobase modifications. At column 13, Langel et al. explicitly contemplate 2-thiopyrimidines as a type of modified nucleobase for use in antisense oligonucleotides. Also, Lin et al. teach nucleosides comprising G-clamp nucleobases, a tricyclic cytosine analog comprising a detectable label and spacer group (see abstract and the definitions of substituents at column 2) and methods of synthesis for these nucleosides using standard synthesis procedures.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make siRNAs comprising modified nucleobases as taught by Fosnaugh et al. with a modified nucleobase that is a 2-thiopyrimidine or a G-clamp as suggested by Langel et al. or Lin et al. It would have further been obvious to make a siRNA wherein each of the sugars of a particular strand are modified with 2'-fluoro modifications and/or every modified nucleobase is inosine. Based on the explicit suggestion by Fosnaugh et al. to use "any non-naturally occurring base" and the

knowledge of modified nucleobases in the art available as exemplified by Langel et al. and Lin et al., one of ordinary skill in the art would recognize the production of siRNAs comprising these nucleobases to be mere design choice made in the course of routine optimization of siRNA structure. Based on the permissive manner used by Fosnaugh et al. in the teaching of siRNAs comprising modified nucleotides, one of ordinary skill in the art would recognize the production of siRNAs comprising a strand fully substituted with 2'-fluoro nucleotides and/or modified nucleobases that are inosine to also be design choice made in the course of routine optimization.

Thus, the invention of claims 1-11, 14, 15, 17, 19, 24, 30-34, 38, 40 and 57-60 would have been obvious, as a whole, at the time the invention was made.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, J. Douglas Schultz, can be reached on 571-272-0763. The central FAX Number is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight

Art Unit: 1635

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Tracy Vivlemore  
Examiner  
Art Unit 1635

TV  
June 21, 2007

A handwritten signature in black ink that reads "Tracy Vivlemore". The signature is fluid and cursive, with "Tracy" on top and "Vivlemore" below it, both starting with a capital letter.